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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/270,152	07/01/94	BOUSSIOTIS	V RPI022

EXAMINER

18M1/1224

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ART UNIT	PAPER NUMBER
1806	15

DATE MAILED: 12/24/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 1/16/96 / 9/20/96

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 48-101 is/are pending in the application.
Of the above, claim(s) 62-96 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) ~~60~~ 48-61, 97-101 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 12
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

★ U.S. GPO: 1996-404-496/40

DETAILED ACTION

1. The Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1806.

2. Applicant's amendment, filed 9/20/96 (Paper No. 14), is acknowledged.
Claims 45-47 have been canceled. Claims 1-44 have been canceled previously.
Claims 48-51, 56, 59, 62, 63, 68 and 71 have been amended.
Claims 97-101 have been added.

Claims 45-101 are pending.

Claims 48-61 97-101 are considered drawn to original elected invention of stimulating proliferation of a T cell which expresses a cytokine receptor gamma chain

Applicant argues that the generic claim 48 links both species of activating and inhibiting T cell responses and considers the species elections, i.e. ,methods for stimulating proliferation of a T cell using an agent which acts extracellularly to inhibit delivery of a signal through a cytokine gamma chains wherein the agent is an anti-γ chain antibody is proper for search purposes only. Applicant affirms this election of Group I, and the species indicated.

Non-elected claims 62-96 are held to be withdrawn from further consideration under 37 CFR 1.142(b).

As indicated below and of record, methods of modulating unresponsiveness by a T cell is rejected under 112, first and second paragraph, because it does not clearly recite the intended endpoint of the elected invention, methods of stimulating T cells.

3. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.
This Action will be in response to applicant's arguments, filed 9/20/96 (Paper No. 14).
The rejections of record can be found in the previous Office Action (Paper No. 11).

4. Applicant's arguments, filed 9/20/96 (Paper No. 14) that it is applicant's positions that the instant methods are drawn to both stimulating and inhibiting T cell activation. The examiner maintains that the title of the invention is not descriptive and should be restricted to the claimed invention.

5. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the form PTO-948 previously sent in Paper No. 11. Applicant is reminded to change the Brief Description of the Drawings in accordance with these changes (see 7. Views).

6. Claims 98-101 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed: ""in a T cell predetermined to be anergic".

The specification as filed does not provide a written description or set forth the metes and bounds of this phrase. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112. Further, it is noted that this phrase is rejected under both 112, first and second paragraphs, below in this Office Action.

Applicant is required to cancel the new matter in the response to this Office action.

7. Claims 48-61 and 97-101are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention as set forth in the previous Office Action (Paper No. 11).

Applicant's arguments, filed 9/20/96 (Paper no. 14), have been fully considered but are not found convincing essentially for the reasons of record set forth in the previous Office Action (Paper No. 11).

Applicant argues that the specification teaches the ordinary artisan how to make and use the claimed invention and that in vivo modulation of response is not a requirement of the claims. However, applicant is reminded of the factors to be considered in determining scope and enablement ; 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented in the specification, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims. See Ex parte Forman, 230 USPQ 546, BPAI, 1986. As the breadth and the intention of the claimed methods do read on normal or primed T cells either ex vivo as well as in vivo. Although applicant relies upon the specification to discloses how to make and to use the claimed methods, there is insufficient objective evidence to support the breadth and the predictability of modulating/inhibiting unresponsiveness of normal or primed T cells either ex vivo as well as in vivo, for the reasons of record. The issue involved is whether or not the evidence of record was based on in vitro studies is generally recognized by those of ordinary skill in the art as being reasonably predictive of success in the practical in vitro and in vivo therapeutic methods encompassed by the instant claims.

Applicant relies upon the holding and dicta in In re Brana 34 USPQ2d 1436 (Fed. Cir. 1995) that their position that it is necessary to supply in vivo clinical data to support claims of the type proposed here. However, Brana was directed to chemical chemotherapeutic compounds structurally similar to other compounds known in the art and for which animal models were art recognized to be predictive of the therapeutic usefulness and which were, as a class, recognized to be effective in treating tumors . The examiner agrees that the it is unnecessary that appellant must prove the ultimate value in humans of their asserted utility. The issue in this case is not whether the general description in the specification of utility, practical or otherwise, for a claimed compound reasonably satisfies the utility requirements of 35 U.S.C. 112, first paragraph and 101, as the Court viewed the case in Brana. Rather the issue here is whether applicant's specification provides insufficient information or nexus which enables any person skilled in the art to use the full scope of the broadly claimed therapeutic methods of modulating or inhibiting unresponsiveness of T cells.

As set forth in the previous Office Action (Paper No. 11), the examiner has set forth both scientific reasoning and evidence as to the unpredictability of modulating or inhibiting unresponsiveness in normal and primed T cells both in vitro and in vivo.

Although applicant notes that the instant methods do not require any specific therapeutic endpoints, applicant also argues that the instant specification enables the use of γ_c stimulatory agents to treat cells with patients from a number of disease states. T cell unresponsiveness does contribute to certain disease states (e.g. Basker et al., PNAS, 1993 cited by applicant);. The instant inventor has disclose that the same or similar description disclosed in the instant specification provides some evidence that after T cell receptor signaling, an event mediated through the γ_c prevents the induction of anergic state, yet this analysis only helps to begin to decipher the molecular mechanisms associated with T cell anergy (Boussiotis et al. Science, 1994; last paragraph).

Therefore, for the reasons of record and set forth above, applicant's arguments are not found persuasive and the rejection is maintained.

8. Claims 98-101are rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are indefinite in the recitation of "in a T cell predetermined to be anergic" because the characteristics of this phrase are not known and ambiguous. Furthermore, the specification as filed has not defined this phrase or set forth clear metes and bounds to determine said limitation.

Applicant has not enabled these claimed methods for the reasons set forth above in section 7. Furthermore, applicant has not provided sufficient teaching or enablement to determine those T cells or conditions wherein "a T cell is predetermined to be anergic". Induction of anergy in many models involves and artificial manipulation of the immune system and cloned cells. Also, there are insufficient means to determine anergy because it is not possible with current methods to physically track T cells of known self peptide/MHC specificity in vivo. Whether an antigen induces anergy or is ignored may depend on the amount of antigen expressed and that affinities of the respond T cell receptors for the relevant peptide/MHC complexes. While anergy may be a mechanism underlying unresponsive states, it is difficult to distinguish between functional inactivation and physical deletion of responding T cells. There is no or insufficient direction or guidance provided to assist one skilled in the art in the selection of T cells predetermined to be anergic in the specification as filed. It appears that undue experimentation would be required of one skilled in the art to practice the method of instant claims using the teaching of the specification alone.

The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter.

9. Claim 48, 56-61 and 98 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 48, 56-61 and 98 are indefinite and ambiguous in the use of "modulating T cell responsiveness" and "such that T cell responsiveness is modulated" in the absence of a clear positive or negative biological effect. .Applicant's arguments, filed 9/20/96 (Paper No. 14) have been fully considered but are not found convincing. Applicant argues that the newly amended claims obviate the previous rejection. However, the instant claims still recite "modulating T cell responsiveness" and "such that T cell responsiveness is modulated". Modulation is not appropriate because modulation can occur both in positive and negative directions and applicant elected methods of stimulating T cells. Also, the endpoint of stimulating signals are ambiguous in the absence of what is the intended or desired biological effect.

The amendments must be supported by the specification so as not to add any new matter.

10. Claims 48-53, 55-58 , 60-61 and 97-100 are rejected under 35 U.S.C. § 102(e) as being anticipated by Plunkett et al. (U.S. Patent No. 5,382,427). Plunkett et al. teaches the use of IL-4 to treat tumors (see entire document).

Applicant's arguments, filed 9/20/96 (Paper No. 14) have been fully considered but are not found convincing. Applicant argues that the reference fails to teach or suggest detecting signaling via a common γ chain or predetermined whether a T cell is unresponsive prior to treatment with IL-4 as required by the amended claims. As applicant asserts in their amendment in response to the rejection under 112, first paragraph; IL-4 meets the claimed methods. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced treatment of tumors with the cytokine IL-4.

11. Claims 48-53, 55-61and 97-100 are rejected under 35 U.S.C. § 102(b) as being anticipated by Lee et al. (U.S. Patent No. 5,017,691). Lee et al. teaches the use of IL-4 to enhance the natural defense against various infections and malignancy (see entire document, particularly column 2, lines 34-66; column 20, lines 51-68).

Applicant's arguments, filed 9/20/96 (Paper No. 14) have been fully considered but are not found convincing. Applicant argues that the reference fails to teach or suggest detecting signaling via a common γ chain or predetermined whether a T cell is unresponsive prior to treatment with IL-4 as required by the amended claims. As applicant asserts in their amendment in response to the rejection under 112, first paragraph; IL-4 meets the claimed methods. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced treatment of tumors with the cytokine IL-4.

12. Claims 48-53, 55-61 and 97-100 are rejected under 35 U.S.C. § 102(a)(e) as being anticipated by Lynch et al. (U.S. Patent No. 5,229,115). Lynch et al. teach the use of IL-7 in the treatment of an individual with cancer of a viral infection by adoptive immunotherapy with T cells in the presence of IL-7 (see entire document, particularly Summary of the Invention).

Applicant's arguments, filed 9/20/96 (Paper No. 14) have been fully considered but are not found convincing. Applicant argues that the reference fails to teach or suggest detecting signaling via a common γ chain or predetermined whether a T cell is unresponsive prior to treatment with IL-4 as required by the amended claims. As applicant asserts in their amendment in response to the rejection under 112, first paragraph; IL-4 meets the claimed methods. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced methods of treating cancer and viral infections with IL-7.

13. Claims 48-53, 59, 61 and 97-100 are rejected under 35 U.S.C. § 102(e) as being anticipated by Grabstein et al. (U.S. Patent No. 5,464,769). Grabstein et al. teach methods of treating microbial infections in a microbially infected mammal by administering IL-7 (see entire document, particularly Summary of the Invention).

Applicant's arguments, filed 9/20/96 (Paper No. 14) have been fully considered but are not found convincing. Applicant argues that the reference fails to teach or suggest detecting signaling via a common γ chain or predetermined whether a T cell is unresponsive prior to treatment with IL-4 as required by the amended claims. As applicant asserts in their amendment in response to the rejection under 112, first paragraph; IL-4 meets the claimed methods. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced treatment of microbial infections with IL-7.

14. Claims 54 and 101 are free of the prior art, however this claim is rejected under 112, first and second paragraphs, set forth above.

15. No claim is allowed.

16. Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

17. Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242 or (703) 305-7939.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee can be reached on (703) 308-2731. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1800 receptionist whose telephone number is (703) 308-0196.

Phillip Gambel, Ph.D.
Patent Examiner
Group 1800
December 12, 1996

LILA FEISEE
SUPERVISORY PATENT EXAMINER
GROUP 1800